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111 - EFFICACY AND SAFETY OF UPADACITINIB INDUCTION THERAPY IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE CROHN'S DISEASE: RESULTS FROM A RANDOMIZED PHASE 3 U- EXCEL STUDY

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Resumen

Introduction: Here we report the results from U-EXCEL (NCT03345849), a phase 3, double-blind, placebo (PBO)-controlled trial that evaluated the efficacy and safety of UPA 45 mg (UPA45) once daily as induction therapy in patients with Crohn’s disease (CD), with an inadequate response or intolerance to conventional therapies or one or more biologics.

Methods: Eligible patients (N = 526) with moderately to severely active CD, defined as average daily stool frequency (SF) ≥ 4 and/or abdominal pain score (APS) ≥ 2, along with a Simple Endoscopic Score for CD (SES-CD) (excluding the narrowing component subscore) ≥ 6 (≥ 4 for subjects with isolated ileal disease) were randomized in a 2:1 to either UPA45 or PBO for 12 weeks (wks). Patients on baseline corticosteroids (CS) initiated a protocolized tapering beginning at wk 4. The co- primary endpoints, clinical remission (per CDAI [CDAI 150] or per SF/APS [average daily SF # 2-point reduction from BL for patients with a BL SES-CD = 4), were evaluated at wk 12. Safety, along with primary and key secondary clinical and endoscopic outcomes were evaluated through wk 12.

Results: BL demographics and characteristics were similar between groups; 45.4% of patients had a history of prior biologic use or failure. At wk 12, significantly more patients receiving UPA45 *vs.* PBO achieved the co-primary endpoints: clinical remission (per CDAI, UPA45 49.5 *vs.* PBO 29.1%; per SF/APS, UPA45 50.7 *vs.* PBO 22.2%) and endoscopic response (UPA45 45.5 *vs.* PBO 13.1%) (p 0.0001 for all endpoints). UPA45 was superior to PBO for most of the ranked secondary endpoints including clinical remission per CDAI and SF/APS at wk 4, CS-free clinical remission per CDAI and SF/APS at wk 12, clinical response (CR-100; 100-point decrease in CDAI from BL at wk 2 and wk 12, and endoscopic remission at wk 12 (p 0.0001 or p 5% of patients) were acne and anaemia among patients treated with UPA, and CD exacerbation among patients in PBO. Serious infections were 1.1% and 1.7% for UPA45 and PBO groups, respectively. Herpes zoster (2.9%) was reported in the UPA45 group, whereas an adjudicated cardiovascular event (0.6%) was reported in the PBO group. No treatment-emergent deaths, malignancies, other opportunistic infections, adjudicated gastrointestinal perforations or adjudicated thrombotic events were reported in either group.

Conclusions: UPA45 induction therapy was superior to PBO in achieving early response, including clinical remission, endoscopic response, and CS-free clinical remission during the U-EXCEL study. UPA45 was well tolerated, with no new safety risks and a safety profile comparable to previous UPA studies.